SUBJECT INDEX

A Acetaminophen	Antipsychotic medication potential	Blood-brain barrier drug-candidate screening
hepatoxicity induced by, 48, 55	5-ht ₆ receptors, 319, 322– 24, 328–30	and, 141 Botulinum, 1–2
reactive metabolites of, 20, 28	Antisense, 319, 327–28, 330 Apolipoprotein E	Branched-DNA signal amplification, 337–38, 347–
Acetylcholine	cholesterol levels and, 105	49
binding pocket models, 435, 439–40 botulinum and, 2	Apoptosis 14-3-3 proteins and, 617, 629–32	Bromobenzene, 48 Bromotrichloromethane, 48,
early studies, 1–3, 6 nicotinic receptors	hypoxia-induced, 529 mitochondrial bioener-	
See Nicotinic acetylcho-	getics and, 353	C
line receptors	Rho and, 472–73	Caco-2, 133-41, 143
physical chemistry of binding, 437–38	Aryl hydrocarbon (Ah) receptor pathway	permeability screening for, 133, 139–41
Acivicin, 31	PAS domain and, 521-27,	automation and, 139-40
Adenosine 5'-triphosphate (ATP)	537 Ascorbic acid synthesis, 23–	immobilized artificial membrane (IAM) chro-
P2X receptors and, 563-75	24	matography, 140
Adenylate cyclase (AC) activity	Atabrine, 20 ATP-synthetase inhibitors,	parallel artificial mem- brane permeation
5-ht, receptor and, 321	364	assay, 140
regulation by opioids,	Autoimmunity	Cancer
390-93	autoimmune hepatitis,	UDP-glucuronosyltransfer-
Aflatoxin, 48	605-6	ases and, 581, 603-5
AIDS	UDP-glucuronosyltransfer-	Carbonic anhydrase, 1
dual protease inhibitor	ases and, 581, 605-6	Carbon tetrachloride, 43–55
therapy for HIV infec- tion, 651–72	Automation, 203	hepatoxic properties of, 43, 45, 51
Alcohols		liver injury, 43-55
sulfation of, 164	В	biotransformation and,
Allostery, 444-48	Bayes theory, 72	48
Allyl formate, 48	Bioenergetics	free radicals and, 48–49
Alzheimer's disease 5-ht ₆ receptors and, 329	apoptosis and, 353 cell signaling and, 353	lipid peroxidation and, 49–50
Amprenavir, 651, 653-55,	mitochondrial, 353-78	potentiation, 50-53
666–68	Bioinformatics, 97, 120, 177,	sympathetic nervous
Anabolic steroids, 24	182, 188	system and, 46-49
Angiogenesis, 295, 303-4	Biotransformation	Carcinogenesis
vascular endothelial growth factor and, 303–4	chemical-induced hepato- toxicity and, 48	UDP-glucuronosyltransfer- ases and, 603–5

Cathepsin K, 193, 197-99, 202 osteoporosis treatment, 197-99 Cell adhesion selectins and myocardial injury and, 283-91 Cell cycle 14-3-3 proteins and, 617 Cell growth hypertrophic Rho and, 472 Cell migration Rho and, 468-69 Cell proliferation Rho and, 471 Cell signaling mitochondrial bioenergetics and, 353 Cheminformatics, 177, 184-85, 188 Chlordecone, 52 Chlorinated methanes carbon tetrachloride, 43 chloroform, 43

liver injury and, 43 mechanism of action, 45 Chloroform, 43, 48-55 biotransformation and, 48 free radicals, 48-50 hepatotoxic properties of, lipid peroxidation and, 49-

50, 55 potentiation, 50-53 Circadian rhythms PAS domains and, 519,

533-37 Clinical trials simulation See Computer simulation

clinical trials Clozapine, 321, 326, 330

Cognition 5-ht, receptors and, 319, 322-24, 328-29 anxiety, 328, 330 depression, 328, 330

dysfunctions, 329-30 memory disorders, 328potential therapeutic indications, 329-30

Combination therapy, 658-

Combinatorial chemistry, 177, 182, 188, 202, 273-79 mixture-based, 273-79

parallel array synthesis approaches, 273-75, 278-79

Computer simulation clinical trials, 209-31 good practices, 213-14

simulation models, 215-17 software, 217-19

Conformation muscarinic receptor, 1, 6-8, 10-12

NMR studies of, 6-12 Creutzfeld-Jakob disease, 636

Crigler-Najjar syndrome, 581, 600-1

Cytochrome c oxidase (COX) inhibitors, 355, 362-64

Cytochrome c oxidoreductase, 360

Cytochrome P450 drug-candidate screening and, 133, 141-44, 150 enzymes

deuterium isotope

effects, 32-33 mechanisms of, 31-33 induction, 143-44

inhibition, 141-43, 649, 653, 655, 659-61, 664-

dual protease inhibitors, 649, 653, 655, 659-61, 664-65 superfamily, 118-19

drug metabolism and, 118 - 19Cytoskeleton, 459, 464-66 actin

> Rho and regulation of, 464-66, 469, 474

Cytotoxicity inhibitors, 357-64, 378 uncouplers, 353-54, 365-78

Deconvolution, 273, 276, 278 iterative, 273, 276, 278 Detoxification glucuronidation, 581-606

Differential displays, 338-39 Dihydrofolate reductase

(DHFR), 1, 11-12 Dimethylnitrosamine, 48

2-4-Dinitrophenol, 366-67, 371

Dioxin aryl hydrocarbon receptor pathway and, 519, 521-

27 DNA sequence variation single nucleotide polymorphism (SNP) and, 97. 102 - 18

Dopamine sulfation of, 164

Down's syndrome comparative genomics and, 122-23

Drug action targets, 1-14 atypical sensitivity and, 10 muscarinic receptor specificity and, 6-14

Drug atypical sensitivity, 10 Drug candidate screening

absorption potential assessment, 139-41 Caco-2 permeability

and, 139-41, 143 biotransformation, 147-49

blood-brain barrier, 141 computer modeling, 149counterscreens, 136 criteria, 135-36 cytochromes P450, 141-44, 150 induction, 143-44 inhibition, 141-43 drug metabolism and, 133, 135 - 51interpretation, 137 pharmacokinetics and, 133, 135-51 See also High-throughput screening; Screening Drug design, 1-14 receptor specificity and, 6-14 Drug development computer simulation clinical trials, 209-31 good practices, 213-14 simulation models, 215-17 software, 217-19 dual protease inhibitors and, 671 modeling and, 67-90 definition, 68 examples, 80-87 exchangeability, 75-76 informative deviations, 77-78 learn-confirm cycles, 67, 69-71 marginal versus conditional, 76-77 pharmacokinetic/pharmacodynamic, 67-68, 72-90 uses, 78-80 Drug discovery cheminformatics, 177, 184-85, 188 combinatorial chemistry,

177, 182, 188, 202, 273-

79

mixture-based, 273-79 parallel array synthesis approaches, 273-75, 278 - 79gene therapy, 177, 186-88 genomics and, 177, 185-86, 188, 193-205 automation, 203 cathepsin K, 193, 197-99, 202 combinatorial chemistry, 202 expressed sequence tags (EST) sequencing, 193-99, 205 functional, 177, 185-86, high-throughput screening and, 193-205 microarrays, 193, 203-4 novel protein sequences, 196-97 "smart" libraries, 194target validation, 193-205 high-throughput screening, 133-51, 177, 180-84, 188, 193-205 5-ht, receptors and, 319-30 antipsychotic medication potential, 319, 322-24, 238-30 medicinal chemistry, 182-83 protein therapeutics, 186proteomics, 177, 179-80, 188, 193, 204-5 target validation, 177-79, 188, 193-205 toxicity evaluation branched DNA signal amplification, 337-38, 347-49 differential displays, 337-39

hybridization microarrays, 335, 337, 340-46 real-time polymerase chain reaction (RT-PCR), 335, 337, 347scintillation proximity, 337-38, 347-49 serial analysis of gene expression (SAGE), 337-38, 346-47 subtractive hybridization, 337, 339-40 Drug interactions HIV protease inhibitors and, 649, 653-56 Drug metabolism cytochrome P450 and, 118-19, 141-44, 150 drug candidate screening and biotransformation and, 147-49 computer modeling, 149-50 cytochrome P450, 141-44, 150 drug concentration in blood, 19-20 metabolites deuterium isotope effects, 32-33 drug-candidate screening and, 147-49 drug-metabolizing enzymes, 22-23 immune responses to, 33 - 34kinetics of drug metabolism in perfused organs and, 25-26 renal toxicity and, 31 suicide enzyme inhibitors, 31-32 toxic chemically reactive, 19-20, 27-34 pharmacogenetics and, 97, 118-20

Drug screening See Drug candidate screening, High-throughput screening, Screening Drug toxicity mitochondrial targets of, 353 - 78Dual protease inhibitors, 649-70 amprenavir, 651, 653-55, 666-68 HIV, 649-70 impact on clinical treatment of, 664-66 indinavir, 650-56, 661-63, 665-68 lopinavir, 669 metabolic drug interactions and, 655-56 nelfinavir, 650-55, 663-69 ritonavir, 650-55, 657-69 saguinavir, 650-60, 665-68 Duchenne muscular dystro-

E Ecosanoids

phy, 300-1

cell therapy for, 300-1

sulfation of, 164 Electrochemical proton gradient, 354-56 Endoplasmic reticulum liver injury chlorinated methanes and, 43-45 Endothelium myocardial injury and, 283-91 nitric oxide and, 284, 289-

selectins and, 283-91 cell adhesion cascade of inflammation and, 284, 290-91

Epoxides, 27, 32

Erythropoeitin-responsive anemias, 302-3 Estrogen

sulfation of, 164 N-Ethyl-N-nitrosurea, 186 Expressed sequence tags (ESTs), 193-99, 205

Extrahepatic

See UDP-glucuronosyltransferase, extrahepatic

14-3-3 proteins, 617-38 antagonists, 637 Creutzfeldt-Jakob disease and, 636 isolated lissencephaly sequence (ILS), 636 ligand interactions, 624-28 Miller-Dieker syndrome (MDS), 636 phosphoserine-mediated interactions, 617, 624-25 properties, 618 regulation of, 634-36 regulation of intracellular signaling, 626-34 Free radicals, 48-50, 55, 353 carbon tetrachloridederived, 49-50, 55 chemical-induced hepatotoxicity and, 48-50 Furosemide, 48

G $G\alpha_{12/13}$, 459, 472, 475–76 GABA, receptors, 431-32, 435, 442 GABA_c receptors, 431-32 Gene regulation tetracycline-inducible retroviral vectors and, 305-7 Gene therapy, 177, 186-87, 295-311 ex vivo approaches, 296 in vivo approaches, 296 muscle stem cell, 307, 309 myoblast-mediated, 295-311 Duchenne muscular dystrophy and, 300 encapsulation of myoblasts and, 310-11 ex vivo gene delivery, 296-305 secretable factors gene delivery, 301-5, 309tetracycline-inducible ret-

roviral vectors, 295, 305-Gene transcription Rho and, 469-71, 474 Genomics, 97-125 chimpanzee, 123-24 comparative, 97, 120-23 synteny, 121-23 drug discovery and, 193automation, 203 cathepsin K, 193, 197-99, 202 combinatorial chemistry, 202 expressed sequence tags (EST) sequencing, 193-99 high-throughput screening, 193-205 microarrays, 193, 203-4 novel protein sequences, 196-97

pharmacogenetics and, 97, 118, 120 proteomics, 193, 204-5 "smart" libraries, 194target validation, 193-205

drug screening See Drug candidate screening; Highthroughput screening; Screening functional, 177-89

human, 97-125

comparative genomics, 97, 120-23 evolution and, 124 synteny and, 121-23 limits of, 124-25 Gilbert's syndrome, 581 Glucuronidation, 581-606 carboxylic acid, 595-96 gastrointestinal tract, 600-1 O-linked, 593 N-, 596 phenanthrene, 593, 595 steroid, 595 Glycine receptors, 431, 435, 442 P-Glycoprotein, 649 Glycoprotein adhesion molecules selectins, 283-91 P-Glycoprotein (PGP) efflux pump, 139-41 G protein-adenylate cyclase pathway, 390-93 G protein-coupled inwardly rectifying K+ channels, 240 G protein-coupled receptor kinases (GRKs), 235-36 G protein-coupled receptors (GPCRs) agonists lysophosphatidic acid (LPA), 459, 463, 465, 467-69, 473 thrombin, 459, 465, 468-69, 471 cross-reactivity of ligands, 201 - 2drug discovery targets, 178, 180, 183-85 gene superfamily, 199-202 melanin-concentrating hormone, 200-1 opioid receptors, 389-415 orexins, 200-1

receptor genes, 405–12 receptor phosphorylation,

399-405

receptor structure, 389-99 opioid receptor signaling and, 389-415 See also Opioid receptors G protein-coupled receptor small, 459 signaling pathways, See also G protein-coupled receptors; Opioid 235 - 62regulator of G protein sigreceptors Growth suppression, 491, naling (RGS) proteins 507-8 and, 235-62 GTPase activating proteins cell types, 240-43 (GAPs), 235-37, 249mechanisms of action. 62, 460 243-44 mechanism of activity, G protein-coupled signal 252-55 transduction, 459-78 mutagenesis, 254-55 Rho-dependent pathways Guanine exchange factors, and, 459-78 apoptosis and, 472-73 Guanine nucleotide dissociabacterial toxins and. tion inhibitors (GDIs), 462-64 460, 462 cell migration and, 468-Guanine nucleotide exchange 69 factors, 460 cell proliferation and, 471 cytoskeleton and, 459, H 464-66, 474 Halothane, 48, 55 effectors, 464 Hemophilia B, 302 gene transcription and, Hepatocarcinogenesis 469-71, 474 oxidative-stress hypothehypertrophic cell sis, 504 growth, 472 peroxisome proliferator-MAP kinase activation induced, 495, 497, 504-7 and, 469-71 Hepatocytes phospholipid metabodrug screening and, 133, lism, 462, 466-67 148 regulators, 460-64 Hepatotoxicity RhoA, 459-60, 465. biotransformation, 48 470, 472-74 chlorinated methanes and. RhoGAPs, 460 43-56 RhoGDI, 460, 462 free radicals and, 48-50. RhoGEF, 459-61 smooth muscle contrachepatocellular regeneration tion, 467-68, 474 and, 43, 53-55 tumor cell invasion and, lipid peroxidation and, 49-467-69 50, 55 G proteins, 389-415 oxidative stress leading to, G protein-adenylate 50, 55 cyclase pathway, 390-93 High-throughput screening heterotrimeric, 459, 467 (HTS), 133-51, 177,

180-84, 188, 193-205, 335, 337 drug discovery and, 193-See also Candidate drug screening; Screening HIV infection dual protease inhibitor therapy for, 649-70 HMG-1, 180 5HT, receptor, 431-32, 435 5-ht₆ receptors antipsychotic medical potential, 319, 322-24, 328-30 antisense oligonucleotides, 319, 327-28, 330 cellular responses, 326-27 cholinergic neurotransmission, 319, 329 knockout mice, 328 learning and memory disorders treatment potential, 319, 322-24, 328-30 localization of mRNA. 324-25 localization of receptor protein, 325-26 molecular biology, 320 molecular pharmacology, 320-22 adenylate cyclase and, 319, 321 potential therapeutic indications, 328-29 selective regulation of agonists and antagonists, 322-24, 328-29 tissue responses, 327 Human Genome Project, 177 Human genomics, 97-125 comparative genomics, 97, 120 - 23synteny and, 121-23 evolution and, 124

limits of, 124-25

microbial pathogens and, 100–2 pharmacogenetics and, 97, 118, 120 See also Genomics Hypoxia response pathway apoptosis and, 529 PAS domains and, 519, 527–33, 537

288-89

Isoniazid, 10, 48

Isolated lissencephaly

sequence, 636

Learning and memory disorders I 5-ht, receptors and, 319, Immobilized artificial mem-322-24, 328-29 brane chromatography, Libraries chemical, 337 140 mixture-based combinato-Immunology, 19, 33-34 Indinavir, 650-56, 661-63, rial, 273-76 665-68 iterative deconvolution Inflammation of soluble, 276 peroxisome proliferatorpositional scanning synactivated receptors and, thetic combinatorial, 276, 491, 497-98, 508-9 278-79 Inherited unconjugated Library synthesis, 273-79 hyperbilirubinemia. Lipid peroxidation, 43, 49-601-5 50 Ion channels hepatotoxicity and, 43, functional organization, 49-50 441-43 Lipinski's Rule, 149-50, 184 ligand-gated, 431-48, Lipolysis, 25 563-75 Lipophilic weak acids, 365opioid receptors and, 393-66 95 Liver injury P2X receptors, 563-75 chlorinated methanes and, structural organization, 440-41 altered sinusoidal circu-Ionophores, 372-73 lation and, 46 Iproniazid, 10 biotransformation and, Ischemia/reperfusion injury 48 selectin inhibitors and, endoplasmic reticulum 283 - 91and, 43-45 free radicals and, 48-50, monoclonal antibodies, 285-87 55 selectins, 283-91 hepatocellular regenerasialyl Lewisx analogs, tion, 43, 53-55

Keratinocyte growth factor-1,

receptor, 389, 410-12

lipid peroxidation and,

mitochondria and, 43-

49-50, 55

45

187

Knockout mice

L

Ketones, 43

potentiation of, 50–53 sympathetic nervous system and, 46–48 Lopinavir, 669 LOV domains, 519, 544 Lysophosphatidic acid (LPA), 459, 463, 465, 467–69, 473

M

Magainin, 273-74 Malaria cytokines and, 101 genomics and, 100-1 tumor necrosis factor and, 101 MAP kinase activation, 469-71 Melanin-concentrating hormone, 200-1 Metabolism UDP-glucuronosyltransferases and, 581-606 Metabolites See Drug metabolism. metabolites: Reactive metabolites Methamphetamine, 48 Microarray gridding (genechip), 179 Microarrays, 193, 203-4, 335, 337, 340-46 Microbial pathogens, 100-2 genomics and, 100-2 malaria, 100-2 multidrug resistance and, 100 Miller-Dieker syndrome, 636 Mitochondria, 353-78 bioenergetics, 353-78 drug toxicity and, 353energy production in, 354-

56

liver injury

chlorinated methanes

and, 43-45, 55

uncouplers of, 353-54, 357, 365-77 poisons, 356-77 inhibitors of ATP-synthase, 364 inhibitors of respiratory chain, 357-64 uncouplers of oxidative phosphorylation, 353-54, 357, 365-77 Mitogen-activated protein (MAP), 459 kinase activation, 469-71 Modeling Bayes theory, 72 drug development and, 67-90 exchangeability, 75-76 informative deviations, 77 - 78marginal versus conditional, 76-77 notation, 71-72 pharmacokinetic/pharmacodynamic, 67, 74-90 defined, 74 statistical, 67-90 Models descriptive, 69, 75, 76 defined, 69 deviation from protocol, 73 - 74empirical, 67, 69-70 defined, 69 mechanistic, 67, 69-70 defined, 69 outcome, 74 pharmacokinetic/pharmacodynamic, 67, 74-90 defined, 74 future needs, 88-90 Molecular toxicology drug screening, 335-50 branched DNA signal amplification, 337-38,

347-49

oxidative phosphorylation,

353-78

differential displays, 337-39 hybridization microarrays, 335, 337, 340-46 real-time polymerase chain reactions (RT-PCR), 335, 337, 347scintillation proximity, 337-38, 347-49 serial analysis of gene expression (SAGE), 337-38, 346-47 subtractive hybridization, 337, 339-40 Monoclonal antibodies, 285directed against selectins, 285-87 Monod-Wyman-Changeux theory, 447-48 Muscarinic receptor, 1-14 conformational variability, 1, 6-8 early studies, 1-14 specificity, 6-14 subtypes, 1 Muscle, 295-311 myoblast-mediated gene therapy and, 295-311 stem cells, 307, 309 See also Myoblast-mediated gene therapy Mycobacterium tuberculosis pentameric mechanosensitive receptor from, 443 Myeloid progenitor inhibitory factor-1, 187 Myoblast-mediated gene therapy, 295-311 Duchenne muscular dystrophy, 296-305 encapsulation of myoblasts and, 310-11 ex vivo gene delivery, 296-305 secretable factors gene delivery, 301-5, 309-11

angiogenesis and, 303–4 erythropoietin-responsive anemias, 302–3 homophilia B, 302 vascular endothelial growth factor, 303–5 fyocardial injury

Myocardial injury selectin and, 283–91 selectin inhibitors and, 283–91

N

Nelfinavir, 650–55, 663–69 Neuropharmacology, 19, 24– 25

NFAT, 248

Nicotinic acetylcholine receptors (nAChRs), 431–48

allosteric transitions of, 444-48

site for potentiation by Ca²⁺, 445

Monod-Wyman-Changeux theory, 447–48

nAChR oligomer, 432–33 nicotinic binding

binding pocket models,

pharmacological diversity of sites, 438-39 physical chemistry of, 437-38

sites at subunit interface, 436–37

subunit structure, 433–36 transmembrane organization, 433–36

Nitric oxide endothelium derived, 284,

289–90 ρ-Nitrophenol sulfaction of, 164

Nuclear magnetic resonance (NMR)

receptor studies using, 1, 6-12

0

Opioid receptors, 389–415 Ca²⁺ mobilization and, 395–97 G protein-adenylate

G protein-adenylate cyclase pathway, 390–93 ion channels and, 393–95 MAP kinase cascades and, 397–99

phospholipid C pathway and, 395-97

receptor genes, 405–12 gene concentration and pharmacological activities, 409–12 gene structure, 407–9

knockout mice, 389, 410-12

mRNA levels, 405–7 receptor phosphorylation, 399–405

desensitization and, 399-403 receptor internalization

and down-regulation and, 403–5

receptor structure, 389–99 signaling, 389–415 See also G protein–cou-

See also G protein—coupled receptors Orexin receptors, 200–1

Orexins, 200–1 feeding behavior and, 200–1

Osteoporosis treatment cathepsin K, 197–99

Oxidative phosphorylation, 353-78 mitochondrial, 353, 357

mitochondrial, 353, 357 uncouplers of, 353–54, 357, 365–77

Oxidative stress hepatotoxicology and, 50, 55

P

Parallel-array synthesis, 273–75, 278–79

Parallel artificial membrane permeation assay (PAMPA), 140 PAS, 519–45

> aryl hydrocarbon (Ah) receptor pathway and, 521–27

basic-helix-loop-helix (bHLH) proteins, 521

circadian response pathway, 533-37

domains, 519-45

hypoxia response pathway and, 527–33, 537

Permeability transition, 353, 356 mitochondrial poisoning

and, 356 Peroxisome proliferatoractivated receptors

(PPARs), 491–50 cell growth and differentiation and, 492–509

fatty acid metabolism and, 492-95, 509

glucose homeostasis, 492– 95, 509

inflammation and, 491, 492-98, 509-9

492–98, 509–9 ligands, 495–99

structure and function of isoforms, 492-95

Peroxisome proliferators (PPs), 491–510

hepatocarcinogenesis induced by, 504–7 oxidative-stress hypothesis, 504–6

response elements, 499–500

Pharmacodynamics, 67–68, 72–90, 209–31, 649 computer simulation clini-

cal trials, 209, 212-31 defined, 68

modeling in drug development, 67-68, 72-90

examples, 80-87 future needs, 88-90 uses, 78-80 **Pharmacogenetics** human genomics and, 97, 118 - 20sulfotransferase, 159-71 Pharmacokinetic/pharmacodynamic drug action model, 212, 216, 218-31 modeling, 67-68, 72-90 drug development and, 67-68, 72-90 hierarchical model approach in, 76-77 Pharmacokinetics computer simulation clinical trials, 209, 212-31 defined, 68 drug-candidate screening and, 133, 144-47 HIV protease inhibitors and, 653-55, 657-70 in vitro screening, 144-45 in vivo screening, 145-47 modeling in drug development and, 67-68, 72-90 examples, 80-87 future needs, 88-90 uses, 78-80 species, strain, and sex differences, 19, 25-27 Phenylpropylamine, 48 Phospholipid metabolism Rho and regulation of, 462, 466-67 Phosphoserine, 617, 624-25 Pirenzipine, 5 Polymerase chain reaction, real-time (RT-PCR), 335, 337 Positional scanning, 273, 276, 278-79 Protein-protein interaction 14-3-3 proteins and, 617-

38

Protein therapeutics, 187–88 Proteomics, 177, 179–80, 193, 204–5 P2X receptors, 563–75 ATP and, 563–75 heteromeric, 563, 573–75 homomeric, 563–73 Pycnodysostosis, 198

heteromeric, 563, 573-75 Reactive metabolites chemical-induced hepatotoxicity and, 19, 27-30, 48 - 50Reactive oxygen species, 50, 355 Real-time polymerase chain reaction (RT-PCR), 335, 337 Receptor phosphorylation, 399-405 opioid desensitization and. 399-403 receptor internalization and down-regulation, 403 - 5Receptors aryl hydrocarbon (Ah), 521-27 early studies, 1, 3-14 G protein-coupled cross-reactivity of ligands, 201-2 drug discovery targets, 178, 180, 183-85 gene superfamily, 199-202 melanin-concentrating hormone, 200-1 opioid receptors, 389-415 orexins, 200-1 receptor genes, 405-12

receptor phosphoryla-

receptor structure, 389-

tion, 399-405

99

muscarinic, 1-14 conformational variability, 1, 6-8 early studies, 1-14 specificity, 6-14 subtypes, 1 nicotinic acetylcholine (nAChRs), 431-48 allosteric transitions of. 444-48 Monod-Wyman-Changeux theory, 447-48 nAChR oligomer, 432nicotinic binding, 436subunit structure, 433transmembrane organization, 433-36 opioid, 389-415 Ca2+ mobilization and, 395-97 G protein-adenylate cyclase pathway, 390ion channels and, 393-MAP kinase cascades and, 397-99 phospholipid C pathway and, 395-97 receptor genes, 405-12 receptor phosphorylation, 399-405 receptor structure, 389signaling, 389-415 orexin, 200-1 perixisome proliferatoractivated (PPARs), 491cell growth and differentiation and, 492-509 fatty acid metabolism and, 492-95, 509 glucose homeostasis. 492-95, 509

inflammation and, 491,

structure and function of

492-98, 509-9

ligands, 495-99

isoforms, 492-95 P2X receptors, 563-75 ATP and, 563-75 heteromeric, 563, 573homomeric, 563-73 Regeneration hepatocellular, 43, 53-55 Regulator of G protein signaling (RGS) proteins, 235-62 chromosomal localization of, 244-45, 248-50 desensitization and, 246discovery of RGS family, 237, 262 gene structure of, 244-45 G protein-coupled receptor signaling in various cell types and, 240-43 intracellular localization of. 248-50 links to other signaling pathways, 257-60 molecular structure of. 250-57 mutagenesis studies of GTPase activating proteins, 254-55 mRNAs of, 245-46 protein function, 237-40 protein structure, 252-53 Renal toxicity, 31 Reserpine serotonin and norepinephrine release and, 24 Retroviral vectors tetracycline-inducible, 295, 305-9 Rho family of proteins G protein-coupled signal transduction and, 459-78 apoptosis and, 472-73

bacterial toxins and. 462-64 cell migration and, 468-69 cell proliferation and, 471 cytoskeleton and, 459, 464-66, 474 effectors, 464 gene transcription and, 469-71, 474 hypertrophic cell growth, 472 MAP kinase activation and, 469-71 phospholipid metabolism, 462, 466-67 regulators, 460-64 RhoA, 459-60, 465, 470, 472-74 RhoGAPs, 460 RhoGDI, 460, 462 RhoGEF, 459-61 smooth muscle contraction, 467-68, 474 tumor cell invasion and. 467-69 Ritonavir, 650-55, 657-69 Rule of Five, 149-50, 184

S
Saquinavir, 650–60, 665–66
Schizophrenia
5-ht₆ receptors and, 329–30
Scintillation proximity
assays, 347–48
Screening

drug candidate screening absorption potential assessment, 139–41 biotransformation, 147– 49 blood-brain barrier, 141 computer modeling, 149–50 counterscreens, 136

criteria, 135-36 cytochromes P450, 141-44, 150 drug metabolism and, 133, 135-51 interpretation, 137 pharmacokinetics and, 133, 135-51 high-throughput (HTS), 133-51, 177, 180-84, 188, 193-205, 279, 335, drug discovery and, 193-205 molecular toxicology drug screening, 335-50 branched DNA signal amplification, 337-38, 347-49 differential displays, 337-39 hybridization microarrays, 335, 337, 340-46 real-time polymerase chain reactions (RT-PCR), 335, 337, 347scintillation proximity. 337-38, 347-49 serial analysis of gene expression (SAGE), 337-38, 346-47 subtractive hybridization, 337, 339-40 positional, 273, 276, 278-79 See also Drug candidate screening; High-throughput screening; Screening Secreted factors gene therapy and, 295, 298, 301-5, 309-11 angiogenesis and, 303-4 Selectin, 283-91

leukocyte-endothelium

injury, 284, 290-91

interaction in reperfusion

P-Selectin glycoprotein ligand-1, 289 Selectin inhibitors, 283-91 protective action of, 283-84, 286-91 ischemia/reperfusion, 285-87 Sequencing expressed sequence tags (EST), 193-99, 205 shotgun, 98-98, 100 Serial analysis of gene expression (SAGE), 337-38, 346-47 Serotonin, 319-30 5-ht₆ receptors, 319-30 sulfation of, 164 Seven transmembrane receptors, 199-202 Sialyl Lewis^x, 283, 286, 288-89 Signal transduction 14-3-3 proteins and, 619, 628-36

G protein-coupled receptors, 389–415 opioid receptors, 389–415 Raf-1-mediated, 629–31 regulator of G protein signaling (RGS) proteins, 235–62

See also G protein-coupled signal transduction; Rho family of proteins Single nucleotide polymor-

phisms (SNP), 97, 102– 18 cancer risk and, 106–17

in a coding region (cSNP),

disease prevention, diagnosis, and treatment strategies, 105

Smooth muscle contraction Rho and, 467–68, 474 Snake venom α-toxins, 432

Solid-phase peptide synthesis, 273-74, 278-79

Spironolactone, 31 Steatosis chlorinated methanes and, 43–45, 47

mechanisms of action, 45 Streptomyces lividans tetrameric potassium channel of, 443

Structure-activity relationships, 183

Subtractive hybridization, 337, 339–40

Suicide enzyme inhibitors, 31–32

Sulfotransferase, 159–71 classification, 162–65 gene expression, 165 nomenclature, 160, 170 SULT gene, 160–62

Sulphonamides, 4 SULT

See under Sulfotransferase Synteny, 121–23 comparative genomics and, 121–23 Down's syndrome and, 122–23

T

TaqMan polymerase chain reaction, 179 Target validation, 177–79, 188, 193–205 cathepsin K, 193, 197–99 EST sequencing, 193–96

EST sequencing, 193–96 novel protein sequences, 196–97 "smart" libraries, 194–96

TCDD differential display studies of, 338–39

Tetracycline, 295, 305–9 Tetracycline-inducible retroviral vectors, 295, 305–

Thalidomide, 26 Thrombin, 459, 465, 468–69 Toxic chemically reactive metabolites, 19, 27–30

Tumor cell invasion Rho and, 468–69

Tumor growth suppression peroxisome proliferators, 507–8

Tumorigenesis

14-3-3 proteins and, 638 Tumor necrosis factor malaria and, 101

U

Ubiquinone, 354–55, 360 UDP-glucuronosyltransferases, 581–606 autoimmunity and, 581, 606 carcinogenesis and, 603–5 detoxification process, 581–83 extrahepatic gene expressions, 595–599 genoprotective role, 603–5 human, 587–606 inherited unconjugated hyperbilirubinemia, 599– 600, 603

365-77

Vascular endothelial growth factor (VEGF), 303-5 gene delivery encoding angiogenic factors, 303-4

Uncouplers, 353-54, 357,

X

Xenobiotic-induced bioenergetic failure, 353 Xenobiotic metabolizing enzymes (XMEs), 521– 27

Xenobiotics

drug screening and, 335-50

Z

Zipper mechanism, 7



CUMULATIVE INDEXES

CONTRIBUTING AUTHORS, VOLUMES 36-40

A

Acosta D Jr, 38:63-96 Alexander RW, 36:281-306 Allen JW, 39:151-73 Amara SG, 39:431-56 Ambudkar SV, 39:361-97 Anders MW, 38:501-37 Anderson SP, 40:491-518 Aposhian HV, 37:397-419 Aschner M, 39:151-73 Augustine GJ, 36:659-701

В

Baker RC, 39:127-50 Bakhle YS, 38:97-120 Balboa MA, 39:175-89 Balsinde J. 39:175-89 Barrett JC, 36:573-96 Bellamy WT, 36:161-83 Bennett CF, 36:107-29 Benovic JL, 38:289-319 Benowitz NL, 36:597-613 Bilsky EJ, 36:379-401 Black J, 36:1-33 Blackburn TP, 40:319-34 Blaschke TF, 37:451-75 Blau HM, 40:295-317 Borges K. 39:221-41 Borjigin J, 39:53-65 Botting RM, 38:97-120 Bradfield CA, 40:519-61 Branchek TA, 40:319-34 Brett CM, 38:431-60 Briggs JM, 37:71-90 Broder S, 40:97-132 Brown JH, 40:459-89

Burchiel SW, 36:131-59 Burgen ASV, 40:1-16 Burns ME, 36:659-701 Burt SK, 36:545-71

C

Catterall WA, 37:361-96 Changeux J-P. 40:431-58 Chaudhuri G, 37:477-515 Choudhuri S, 39:267-94 Clapham DE, 37:167-203 Collins MD, 39:399-430 Collman GW, 36:573-96 Conn PJ, 37:205-37 Corringer P-J, 40:431-58 Corton JC, 40:491-518 Costa E, 38:321-50 Costa LG, 38:21-43 Coyle JT, 36:83-106 Crooke ST, 36:107-29 Croxatto HB, 36:47-81

D

Dalton TP, 39:67-101 Davila DR, 36:131-59 Davila JC, 38:63-96 DeBello WM, 36:659-701 Debouck C. 40:193-208 Dekant W. 38:501-37 Dennis EA, 39:175-89 Dessauer CW, 36:461-80 De Vries L, 40:235-71 Dey S, 39:361-97 Dingledine R, 39:221-41 Dray A, 36:253-80 Dunham EW, 37:53-69

\mathbf{E}

Elenko E. 40:235-71 Elliott JD, 40:177-91 Erickson JW, 36:545-71 Evans CJ, 36:379-401 Exton JH, 36:481-509

Farquhar MG, 40:235-71 Felder CC, 38:179-200 Fischer T, 40:235-71 Fisher JW, 38:1-20 Flexner C, 40:651-76 Fu H, 40:619-49

G

Giacomini KM, 38:431-60 Gibbs JB, 37:143-66 Gillette JR, 40:19-41 Gilman AG, 36:461-80 Glass M, 38:179-200 Goldstein A, 37:1-28 Gottesman MM, 39:361-97 Griendling KK, 36:281-306 Gu Y-Z, 40:519-61 Gudermann T, 36:429-59 Guengerich FP, 39:1-17

H

Halmes NC, 37:91-117 Hammond HK, 39:343-60 Hefti F. 37:239-67 Heinrich M. 38:539-65 Hobbs AJ, 39:191-220 Hockerman GH, 37:361-96 Hoffman AR, 38:45-61

Hogenesch JB, 40:519–61 Holford NHG, 40:209–34 Holsapple MP, 36:131–59 Hosokawa M, 38:257–88 Houghten RA, 40:273–82 Hoyer PB, 36:307–31 Hrycyna CA, 39:361–97 Huff J, 36:573–96

I Insel PA, 39:175–89, 343–60 Ito K, 38:461–99 Iwatsubo T, 38:461–99

J Joad JP, 37:29–52 Johnson BD, 37:361–96 Johnson DG, 39:295–312

K

Kalkbrenner F, 36:429–59 Kaminski NE, 36:131–59 Kanamitsu S, 38:461–99 Karras JG, 36:131–59 Kastrissios H, 37:451–75 Kimelberg HK, 39:151–73 Kimko HC, 40:209–34 Klaassen CD, 39:267–94 Kobilka BK, 38:351–73 Kramer RE, 39:127–50 Krupnick JG, 38:289-319

L
Lai J, 36:379–401
Lasségue B, 36:281–306
Lau SS, 38:229–55
Law P-Y, 40:389–430
Ledbetter JA, 36:131–59
Lefer DJ, 40:283–94
Lemasters JJ, 37:327–38
Le Moal M, 36:359–78
Le Novère N, 40:431–58
Li C, 36:185–201
Li X, 39:53–65
Liehr JG, 36:203–32
Lipton SA, 38:159–77
Liu J, 39:267–94

Loh HH, 40:389–430 LoPachin RM, 39:151–73 Lukas SE, 36:333–57

M

Maines MD, 37:517–54
Mao GE, 39:399–430
Marcus R, 38:45–61
Marrone TJ, 37:71–90
Masters SC, 40:619–49
McCammon JA, 37:71–90
Melchert RB, 38:63–96
Metcalf B, 40:193–208
Meyer UA, 37:269–96
Miller RJ, 38:201–27
Moncada S, 39:191–220
Monks TJ, 38:229–55
Monteleone JPR, 40:209–34
Myers MG Jr, 36:615–58
Myers SJ, 39:221–41

N

Nagata K, 40:159–76 Nakajima Y, 38:461–99 Nathan L, 37:477–515 Neal RA, 36:35–46 Neer EJ, 37:167–203 North RA, 40:563–80

0

Ohlstein EH, 40:177–91 Oliff A, 37:143–66 Ortiz de Montellano BR, 38:539–65 Otterness DM, 39:19–52 Ozawa CR, 40:295–317

p

Pastan I, 39:361–97 Peck CC, 40:209–34 Peoples RW, 36:185–201 Peterson BZ, 37:361–96 Pettit DL, 36:659–701 Piazza PV, 36:359–78 Pin J-P, 37:205–37 Pinkerton KE, 37:29–52 Plaa GL, 40:43–65 Polson JB, 36:403–27 Porreca F, 36:379–401 Post SR, 39:343–60 Pratt WB, 37:297–326 Puga A, 39:67–101 Pumford NR, 37:91–117

R

Ramachandra M, 39:361–97 Ramos KS, 39:243–65 Regunathan S, 36:511–44 Reis DJ, 36:511–44 Robbins A, 36:47–81 Robles M, 38:539–65 Rodan GA, 38:375–88 Rodriguez E, 38:539–65 Rodriguez RJ, 38:63–96 Rohrer DK, 38:351–73 Ruffolo RR Jr, 40:177–91

S

Safe SH, 38:121-58 Sagi SA, 40:459-89 Sah VP. 40:459-89 Satoh T. 38:257-88 Schatz AR, 36:131-59 Schieven GL, 36:131-59 Schultz G, 36:429-59 Schweizer FE, 36:659-701 Seal RP, 39:431-56 Seasholtz TM, 40:459-89 Sheiner L, 40:67-96 Shertzer HG, 39:67-101 Sibley DR, 39:313-41 Simonian NA, 36:83-106 Sipes IG, 36:307-31 Snyder SH, 39:53-65 Spitz IM, 36:47-81 Springer ML, 40:295-317 Starkov AA, 40:353-88 Stauber A, 40:491-518 Steimer J-L, 40:67-96 Strada SJ, 36:403-27 Strassburg CP, 40:581-618 Streit WJ, 39:151-73 Strosberg AD, 37:421-50

Stuehr DJ, 37:339–59 Subramanian RR, 40:619–49 Sugiyama Y, 38:461–99 Sunahara RK, 36:461–80 Surprenant A, 40:563–80 Szumlanski CL, 39:19–52

T Thummel KE, 38:389–430 Thurman RG, 37:327–38 Tukey RH, 40:581–618

U Ulrich RG, 40:335-52 Urban L, 36:253-80

V Vanderah TW, 36:379–401 Vane JR, 38:97–120 Venter JC, 40:97–132

W Walker CL, 39:295–312 Wallace KB, 40:353–88 Waring JF, 40:335–52 Wei L-N, 37:119–41 Weight FF, 36:185–201 Weinshilboum RM, 39:19–52 West JE, 38:539–65

White MF, 36:615–58 White RE, 40:133–57 Whitlock JP Jr, 39:103–25 Wilkinson GR, 38:389–430 Witschi H, 37:29–52 Wolff MS, 36:573–96 Wong YH, 40:389–430 Woosley RL, 36:233–52

Y Yager JD, 36:203–32 Yamazoe Y, 40:159–76

Z Zaki PA, 36:379–401 Zanger UM, 37:269–96 Zhang L, 38:431–60 Zheng B, 40:235–71 Zimmerman BG, 37:53–69

CHAPTER TITLES, VOLUMES 36-40

Receptor Gene Expression

PREFATORY		
Pharmacology		
A Personal View of Pharmacology	J Black	36:1-33
A Rewarding Research Pathway	A Goldstein	37:1-28
A Quest for Erythropoietin Over Nine Decades	JW Fisher	38:1-20
Targets of Drug Action	A Burgen	40:1-16
Toxicology		
A Career in Toxicology	RA Neal	36:35-46
Laboratory of Chemical Pharmacology, National Heart, Lung, and Blood Institute, NIH: A Short History	JR Gillette	40:19–41
Chlorinated Methanes and Liver Injury: Highlights of the Past 50 Years	GL Plaa	40:43–65
GENERAL TOPICS IN PHARMACOLOGY AND TOXIC Receptors	COLOGY	
Angiotensin Receptors and Their Therapeutic	KK Griendling, B Lasségue,	36:281-306
Implications	RW Alexander	50.201 500
Central Role of Peroxisome Proliferator-Activated Receptors in the Actions of Peroxisome	JC Corton, SP Anderson, A Stauber	40:491–518
Proliferators Opioid Receptor Types and Subtypes: The δ Receptor as a Model	PA Zaki, EJ Bilsky, TW Vanderah, J Lai, CJ Evans, F Porreca	36:379–401
Diversity and Selectivity of Receptor-G Protein Interaction	T Gudermann, F Kalkbrenner, G Schultz	36:429-59
Imidazoline Receptors and Their Endogenous Ligands	S Regunathan, DJ Reis	36:511-44
Pharmacology and Functions of Metabotropic Glutamate Receptors	PJ Conn, J-P Pin	37:205–37
The Role of the hsp90-Based Chaperone System in Signal Transduction by Nuclear Receptors and Receptors Signaling via Map Kinase	WB Pratt	37:297-326
Structure and Function of the B3-Adrenergic Receptor	AD Strosberg	37:421-50
Cannabinoid Receptors and Their Endogenous Agonists	CC Felder, M Glass	38:179–200
Presynaptic Receptors	RJ Miller	38:201-27
From GABAA Receptor Diversity Emerges A Unified Vision of GABAergic Inhibition	E Costa	38:321-50
Insights from In Vivo Modification of Adrenergic	DK Rohrer, BK Kobilka	38:351-73

Genetic Regulation of Glutamate Receptor Ion	SJ Myers, R Dingledine,	39:221-41
New Insights into Dopaminergic Receptor Function	K Borges DR Sibley	39:313-41
Using Antisense and Genetically Altered Animals		
5-HT ₆ Receptors as Emerging Targets for Drug Discovery	TA Branchek, TP Blackburn	40:319–34
Nicotinic Receptors at the Amino Acid Level	P-J Corringer, N Le Novére, J-P Changeux	40:431–58
Pharmacology of Clonded P2X Receptors	RA North, A Surprenant	40:563-80
Synaptic Functions		
Insulin Signal Transduction and the IRS Proteins	MG Myers Jr, MF White	36:615-58
Exocytosis: Proteins and Perturbations	GJ Augustine, ME Burns, WM DeBello, DL Pettit, FE Schweizer	36:659–701
Molecular Determinants of Drug Binding and Action on L-Type Calcium Channels	GH Hockerman, BZ Peterson, BD Johnson, WA Catterall	37:361–96
Signal Transduction in Environmental Neurotoxicity	LG Costa	38:21-43
Inhibition of Nitric Oxide Synthase as a Potential Therapeutic Target	AJ Hobbs, A Higgs, S Moncada	39:191–220
Redox Regulation of <i>c-Ha-ras</i> and Osteopontin Signaling in Vascular Smooth Muscle Cells: Implications in Chemical Atherogenesis	KS Ramos	39:243-65
Cyclins and Cell Cycle Checkpoints	DG Johnson, CL Walker	39:295-312
The Regulator of G Protein Signaling Family	L De Vries, B Zheng, T Fischer, E Elenko, MG Farquhar	40:235-71
Pharmacology of Selectin Inhibitors in Ischemia/ Reperfusion States	DJ Lefer	40:283-94
The Role of Rho in G Protein Coupled Receptor Signal Transduction	VP Sah, TM Seasholtz, SA Sagi, JH Brown	40:459-89
14-3-3 Proteins: Structure, Function, and Regulations	H Fu, RR Subramanian, SC Masters	40:619-49
Enzymes		
Complexity and Diversity of Mammalian Adenylyl Cyclases	RK Sunahara, CW Dessauer, AG Gilman	36:461-80
Regulation of Phosphoinositide Phospholipases by Hormones, Neurotransmitters, and Other Agonists Linked to G Proteins	JH Exton	36:481–509
The Heme Oxygenase System: A Regulator of Second-Messenger Gases	MD Maines	37:517–54
The Mammalian Carboxylesterases: From Molecules to Functions	T Satoh, M Hosokawa	38:257-88
The Role of Receptor Kinases and Arrestins in G Protein-Coupled Receptor Regulation	JG Krupnick, JL Benovic	38:289-319
Methylation Pharmacogenetics: Catechol O- Methyltransferase, Thiopurine Methyltransferase, and Histamine N-Methyltransferase	RM Weinshilboum, DM Otterness, CL Szumlanski	39:19–52
Regulation and Inhibition of Phospholipase A ₂	J Balsinde, MA Balboa, PA Insel, EA Dennis	39:175-89
Human UDP-Glucuronosyltransferases: Metabolism, Expression, and Disease	RH Tukey, CP Strassburg	40:581–618

Chemical Agents		
Progress in Antisense Oligonucleotide Therapeutics	ST Crooke, CF Bennett	36:107-29
Pharmacology of Nicotine: Addiction and Therapeutics	NL Benowitz	36:597–613
Protein Targets of Xenobiotic Reactive Intermediates	NR Pumford, NC Halmes	37:91-117
G Protein Beta-Gamma Subunits	DE Clapham, EJ Neer	37:167-203
Pharmacology of Neurotrophic Factors	F Hefti	37:239-67
Structure-Function Aspects in the Nitric Oxide Synthases	DJ Stuehr	37:339–59
Enzymatic Methylation of Arsenic Species and Other New Approaches to Arsenic Toxicity	HV Aposhian	37:397–419
The Pharmacology and Toxicology of Polyphenolic- Glutathione Conjugates	TJ Monks, SS Lau	38:229-55
Ethnopharmacology of Mexican Asteraceae (Compositae)	M Heinrich, M Robles, JE West, BR Ortiz de Montellano, E Rodriguez	38:539–65
The Pineal Gland and Melatonin: Molecular and Pharmacologic Regulation	J Borjigin, X Li, SH Snyder	39:53–65
Regulation of Gene Expression by Reactive Oxygen	TP Dalton, HG Shertzer, A Puga	39:67–101
Cytotoxicity of Short-Chain Alcohols	RC Baker, RE Kramer	39:127-50
Metallothionein: An Intracellular Protein to Protect Against Cadmium Toxicity	CD Klaassen, J Liu, S Choudhuri	39:267-94
Teratology of Retinoids	MD Collins, GE Mao	39:399-430
Biotransformation		
Molecular Mechanisms of Genetic Polymorphisms of Drug Metabolism	UA Meyer, UM Zanger	37:269–96
In Vitro and In Vivo Drug Interactions Involving Human CYP3A	KE Thummel, GR Wilkinson	38:389-430
Glutathione-Dependent Bioactivation of Haloalkenes	MW Anders, W Dekant	38:501-37
Cytochrome P-450 3A4: Regulation and Role in Drug Metabolism	FP Guengerich	39:1–17
Induction of Cytochrome P4501A1	JP Whitlock Jr	39:103-25
Pharmacokinetics/Toxicokinetics Role of Organic Cation Transporters in Drug	L Zhang, CM Brett,	38:431-60
Absorption and Elimination Biochemical, Cellular, and Pharmacological Aspects of the Multidrug Transporter	KM Giacomini SV Ambudkar, S Dey, CA Hrycyna, M Ramachandra, I Pastan, MM Gottesman	39:361–97
Mitochondrial Targets of Drug Toxicity	KB Wallace, AA Starkov	40:353-88
Cancer and Carcinogenesis		
P-Glycoproteins and Multidrug Resistance	WT Bellamy	36:161-83
Molecular Mechanisms of Estrogen Carcinogenesis	JD Yager, JG Liehr	36:203-32
The Potential of Farnesyltransferase Inhibitors as Cancer Chemotherapeutics	JB Gibbs, A Oliff	37:143-66
Interactions Between Hormones and Chemicals in Breast Cancer	SH Safe	38:121–58
Clinical Therapeutics		
Medication Compliance as a Feature in Drug Development	H Kastrissios, TF Blaschke	37:451-75
Dual Protease Inhibitor Therapy in HIV-Infected Patients: Pharmacologic Rationale and Clinical Benefits	C Flexner	40:651–76

Drug Development Science		
Structure-Based Drug Design: Computational	TJ Marrone, JM Briggs,	37:71-90
Advances	JA McCammon	
Parallel Array and Mixture-Based Synthetic Combinatorial Chemistry: Tools for the Next Millennium	RA Houghten	40:273–82
A Novel Means of Drug Delivery: Myoblast- Mediated Gene Therapy and Regulatable Retroviral Vectors	CR Ozawa, ML Springer, HM Blau	40:295–317
SYSTEMS		
Immune System/Inflammation		
Molecular Mechanisms of Toxicant-Induced Immunosuppression: Role of Second Messengers	MP Holsapple, JG Karras, JA Ledbetter, GL Schieven, SW Burchiel, DR Davila, AR Schatz, NE Kaminski	36:131–59
Cyclooxygenases 1 and 2	JR Vane, YS Bakhle, RM Botting	38:97-120
Central Nervous System		
Oxidative Stress in Neurodegenerative Diseases	NA Simonian, JT Coyle	36:83-106
Lipid vs Protein Theories of Alcohol Action in the Nervous System	RW Peoples, C Li, FF Weight	36:185–201
New Pharmacological Strategies for Pain Relief	A Dray, L Urban	36:253-80
CNS Effects and Abuse Liability of Anabolic- Androgenic Steroids	SE Lukas	36:333–57
Pathophysiological Basis of Vulnerability to Drug Abuse: Role of an Interaction Between Stress, Glucocorticoids, and Dopaminergic Neurons	PV Piazza, M Le Moal	36:359–78
Glial Cells in Neurotoxicity Development	M Aschner, JW Allen, HK Kimelberg, RM LoPachin, WJ Streit	39:151-73
Excitatory Amino Acid Transporters: A Family in Flux	RP Seal, SG Amara	39:431–56
Molecular Mechanisms and Regulation of Opiod Receptor Signaling Autonomic Nervous System	P-Y Law, YH Wong, HH Loh	40:389–430
β-Adrenergic Receptors and Receptor Signaling in Heart Failure	SR Post, HK Hammond, PA Insel	39:343-60
Cardiovascular System	DI W	26 222 52
Cardiac Actions of Antihistamines Cyclic Nucleotide Phosphodiesterases and Vascular Smooth Muscle	RL Woosley JB Polson, SJ Strada	36:233–52 36:403–27
Tissue Renin-Angiotensin Systems: A Site of Drug Action?	BG Zimmerman, EW Dunham	37:53-69
Reperfusion Injury After Liver Preservation for Transplantation	JJ Lemasters, RG Thurman	37:327–38
Endocrine System		
Antiprogestins: Mechanism of Action and Contraceptive Potential	IM Spitz, HB Croxatto, A Robbins	36:47-81
Assessment of Follicle Destruction in Chemical- Induced Ovarian Toxicity	PB Hoyer, IG Sipes	36:307-31
Estrogens and Atherosclerosis	L Nathan, G Chaudhuri	37:477-515

Growth Hormone As Therapy for Older Men and Women	R Marcus, AR Hoffman	38:45-61
Mechanism of Action of Biophosphates	GA Rodan	38:375-88
Pulmonary System		
The Toxicology of Environmental Tobacco Smoke	H Witschi, JP Joad, KE Pinkerton	37:29–52
Microbial Systems		
Structural Mechanisms of HIV Drug Resistance	JW Erickson, SK Burt	36:545-71
Neuronal Injury Associated with HIV-1: Approaches to Treatment	SA Lipton	38:159–77
MISCELLANEOUS		
Techniques		
Transgenic Animals as New Approaches in Pharmacological Studies	L-N Wei	37:119–41
Predictive Value of In Vitro Model Systems in Toxicology	JC Davila, RJ Rodriguez, RB Melchert, D Acosta Jr	38:63-96
Quantitative Prediction of In Vivo Drug Clearance and Drug Interactions from In Vitro Data on Metabolism, and Together with Binding and Transport	K Ito, T Iwatsubo, S Kanamitsu, Y Nakajima, Y Sugiyama	38:461-99
The Impact of Genomics-Based Technologies on Drug Safety Evaluation	JF Waring, RG Ulrich	40:335–52
Environmental Toxicity		
The PAS Superfamily: Sensors of Environmental and Developmental Signals	Y-Z Gu, JB Hogenesch, CA Bradfield	40:519–61
Risk Assessment		
Breast Cancer and Environmental Risk Factors: Epidemiological and Experimental Findings	MS Wolff, GW Collman, JC Barrett, J Huff	36:573–96
PHARMACOLOGY AND TOXICOLOGY IN THE NEW MILLENNIUM		
Pharmacokinetic/Pharmacodynamic Modeling in Drug Development	LB Sheiner, J-L Steimer	40:67–96
Sequencing the Entire Genomes of Free-Living Organisms: The Foundation of Pharmacology in the New Millenium	S Broder, JC Venter	40:97-132
High-Throughput Screening in Drug Metabolism and Pharmacokinetic Support of Drug Discovery	RE White	40:133-57
Pharmacogenetics of Sulfotransferase	K Nagata, Y Yamazoe	40:159-76
Drug Discovery in the Next Millennium	EH Ohlstein, RR Ruffolo Jr, JD Elliott	40:177-91
The Impact of Genomics on Drug Discovery	C Debouck, B Metcalf	40:193-208
Simulation of Clinical Trials	NHG Holford, HC Kimko, JPR Monteleone, CC Peck	40:209-34

